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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,827	10/15/2001	Johannes Maria Franciscus Gerardus Aerts	294-32 DIVII/CON	4648

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EXAMINER	
PROUTY, REBECCA E	
ART UNIT	**PAPER NUMBER**
1652	9

DATE MAILED: 10/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/977,827	Aerts
Examiner	**Art Unit**
Rebecca Prouty	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 8, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above, claim(s) *15-29 and 31* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-14 and 30* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicant's election without traverse of Group I, Claims 1-14 and 30 in Paper No. 9 is acknowledged.

Claims 15-29 and 31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 9.

Claims 1-14 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and specification. It is particularly noted that Claims 1-4 recite the amino acid and nucleotide sequences of Figs 1 or 2. See particularly 37 CFR 1.821(d).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-14 and 30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 and 23 of U.S. Patent No. 5,928,928. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1-14 and 30 of the instant application and Claims 1-14 and 23 of U.S. Patent No. 5,928,928 are both directed to the human chitinases of SEQ ID NOS:4 and 6, pharmaceutical compositions thereof, non-pharmaceutical compositions thereof (including cell media, cosmetics, dental compositions, and food), chitin-based articles comprising said chitinases and a diagnostic kit comprising said

chitinases. The claims differ in that claims 1-14 and 30 of the instant application further include a variety of variants of said human chitinases in addition to the human chitinases of SEQ ID NOS:4 and 6. Thus, Claims 1-14 and 30 of the instant application are generic to all that is recited in Claims 1-14 and 23 of U.S. Patent No. 5,928,928. That is, Claims 1-14 and 23 of U.S. Patent No. 5,928,928 fall entirely within the scope of Claims 1-14 and 30 of the instant application or, in other words, Claims 1-14 and 30 of the instant application are anticipated by Claims 1-14 and 23 of U.S. Patent No. 5,928,928.

Claims 1-4 (upon which Claims 5-14 and 30 depend) are indefinite in the recitation of "essentially corresponding to" as it is unclear how many changes can be made within the recited sequence and still be included within this phrase. While page 12 of the specification teaches that generally the changes will be less than 30% or the total number of amino acids or nucleotides in the recited sequences, there is nothing which indicates that this term is limited thereto. For purposes of examination this phrase is interpreted to mean at least 70% identity to

Claim 1 (upon which Claims 2-14 and 30 depend) are indefinite in the recitation of "modified form of said human chitinase having a substantially similar chitin-hydrolyzing activity" While page 13, lines 6-15 of the specification teaches

that this terminology "intends to embrace variants whose sequence differs significantly from the sequences shown in Figs 1 and 2 but which yet have similar chitinase activity" it is unclear what the scope of the term "variant" or "modified form" embraces, i.e., must another chitinase have some minimum level of structural similarity to the chitinases of Figs 1 or 2 to be a "variant" or "modified form" thereof or does this phrase encompass any chitinase having a "substantially similar chitin-hydrolyzing activity" (see page 13, lines 16-21 for definition) even if it has no structural similarity at all.

Claim 11 is indefinite in the recitation of "cosmetic (e.g. body lotion)", "dental (e.g. tooth paste, mouth rinse)", and "food product (e.g. milk, cheese and other dairy products) as the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 30 is indefinite in the recitation "a conventional component of diagnostic kits for detecting an antigen or antibody" as it is unclear what things would be considered "conventional components".

Claims 1, 5-14 and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 5-14 and 30 are directed to polypeptides corresponding to SEQ ID NOS:4 and 6 and variants thereof having substantially similar chitin-hydrolyzing activity (broadest reasonable interpretation being any chitinase have substantially similar chitin-hydrolyzing activity). Claims 1, 5-14 and 30 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from SEQ ID NOS:4 and 6 including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue in SEQ ID NOS:4 and 6 and fragments of SEQ ID NOS:4 and 6 that have not been disclosed in the specification. No description has been provided of the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NOS:4 and 6 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the structure of all the polypeptide sequences derived from SEQ ID NOS:4 and 6, including fragments and variants within the scope of the claimed genus.

Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being a chitinase. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-14 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling the human chitinases of SEQ ID NOS: 4 or 6 or chitinases encoded by nucleic acids which will hybridize to the nucleic acids of SEQ ID NOS: 3 or 5 under specific stringent conditions, does not reasonably provide enablement for any chitinase "essentially corresponding" to SEQ ID NOS:4 or 6 or "having substantially similar chitin-hydrolyzing activity" thereto. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1-14 and 30 are so broad as to encompass any chitinase "essentially corresponding" to SEQ ID NOS:4 or 6 or "having substantially similar chitin-hydrolyzing activity" thereto. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of chitinases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of two variants of a single chitinase and the encoding nucleic acids therefor.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in

any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any chitinase "essentially corresponding" to SEQ ID NOS:4 or 6 or "having substantially similar chitin-hydrolyzing activity" thereto because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting chitinase activity; (B) the general tolerance of chitinases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any chitinase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including chitinases having an enormous number of amino acid modifications of the chitinases of

SEQ ID NOS: 4 or 6. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of chitinases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 7 recites the inclusion of a human β-1,3-glucanase in the human chitinase composition. However, at the time of filing the instant application there were no known human β-1,3-glucanases nor any showing of β-1,3-glucanase activity in any human cell line or tissue sample found in the prior art or in applicants specification. As such there is no expectation that humans even produce such an enzyme and it would take undue experimentation to use the claimed method as it would require undue experimentation to make a human β-1,3-glucanase.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Overdijk et al.

Overdijk et al. teach the isolation of a human chitinase and compositions thereof.

Claims 1-4 and 8 are rejected under 35 U.S.C. 102(a) as being anticipated by Renkema et al.

Renkema et al. teach the isolation of 50 kDa and 39 kDa forms of human chitinase identical the chitinases of Figures 1 and 2 and compositions thereof.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Renkema et al.

Renkema et al. teach a human chitinase and teach Gaucher's disease patients exhibit a several hundred fold increase in the levels of this in plasma Renkema et al. further teach an antibody to the human chitinase. As such one of skill in of ordinary skill in the art would have found it obvious to make a kit for the diagnosis of Gaucher's disease which includes the chitinase antibody of Renkema et al., the protein of Renkema et al. as a positive control. and a component which detects the binding of an antibody to its antigen.

Claims 5, 6, 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Renkema et al. or Overdijk et al. in view of Davies et al. or Pope et al.

Renkema et al. and Overdijk et al. each teach a human chitinase and suggest that this protein is important in defense against pathogen infection.

Davies et al. and Pope et al. each teach that mycolytic enzymes, such as chitinases, alone or in combination with other antifungal compounds are useful for the treatment of fungal infections. They teach that these enzymes degrade the fungal cell wall and inhibit fungal growth and/or enhance the activity

of other antifungal agents by increasing the access of such agents to the fungal cell interior.

Therefore, it would have been obvious to make pharmaceutical compositions of the protein of Renkema et al. and Overdijk et al. or to combine the proteins of Renkema et al. and Overdijk et al. with products in which the inhibition of fungal activity would be desirable. One of skill in the art would have clearly been aware that inhibition of fungal activity would be desirable in products including culture media, cosmetics, dental products and food products and thus it would have been obvious to one of skill in the art to make culture media, cosmetics, dental products and food compositions of the proteins of Renkema et al. and Overdijk et al. One of ordinary skill in the art would have been motivated to do so as the protein of Renkema et al. and Overdijk et al. would have been reasonably expected to be less likely to induce an adverse immune response/allergenic reaction as it is a protein naturally produced by humans.

Claims 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Renkema et al. or Overdijk et al in view of Wheatley et al. (US Patent 4,933,185).

Renkema et al. and Overdijk et al. are discussed above.

Wheatley et al. teach a controlled drug release system comprising a microcapsule of a polysaccharide polymer and a

enzyme which can degrade said polymer encapsulated within said microcapsule. Wheatley teach that polymer/enzyme pair can be chitin and chitinase (see column 3, lines 35-38) and teach that enzymes which do not provoke an immune response are preferable (see Claim 14).

Therefore, it would have been obvious to make a controlled drug release system comprising a microcapsule of chitin and the protein of Renkema et al. or Overdijk et al. One of ordinary skill in the art would have been motivated to do so as the protein of Renkema et al. and Overdijk et al. would have been reasonably expected to be less likely to induce an immune response than other known chitinases as it is a protein naturally produced by humans.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652